EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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GMP/GDP Inspectors Working group

Concept paper on revision of Annex 15 of the GMP guide

Draft

Adoption by GMP/GDP IWG for release for consultation	October 2012
Start of public consultation	27 November 2012
End of consultation (deadline for comments)	28 February 2013

The proposed guideline will replace the existing Annex 15

Comments should be provided using this template. The completed comments form should be sent to ADM-GMDP@ema.europa.eu

Keywords	**Annex 15, validation**

1. Introduction

Annex 15 was originally published in September 2001 and since then there have been significant changes in the GMP environment with the incorporation of ICH Q9 and Q10. In addition, the Quality Working Party (QWP) is in the process of updating its guideline on Process Validation and there has been advancement in manufacturing technology through the introduction of Process Analytical Technology (PAT) and continuous manufacture concept. There have also been many changes to other chapters and Annexes in the GMP guide, which may have an impact on Annex 15 and therefore a review on this annex is required.

2. Problem statement

Since Annex 15 was published in 2001 the manufacturing and regulatory environment has changed significantly and an update is required to this annex to reflect this changed environment.

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3. Discussion (on the problem statement)

Although the current version of Annex 15 refers to the concept of risk assessment this activity has been further developed through the introduction of ICH Q9 and further guidance needs to be incorporated into the annex. The concepts in ICH Q9 together with those in ICH Q8 and Q10 have triggered the revision of QWP's Guideline on Process Validation and new guidance needs to be incorporated into Annex 15, including the inclusion of continuous process verification for products subject to an 'enhanced' approach to pharmaceutical development.

Manufacturing technology has developed further over the last 10 years in terms of the complexity of equipment and Annex 15 needs to be updated to ensure that it addresses these changes.

There have also been many changes to GMP and Annex 15 needs to take account of these changes to ensure consistency of requirements. This will include new guidance and also the removal of text that has been superseded or included elsewhere in the GMP Guide. Though not a comprehensive listing, some of the main GMP changes include:

- New text on change control in Chapter 1.
- The implication of Product Quality Reviews on validation activities.
- The work that is on-going to revise the requirements for dedicated facilities in Chapters 3 and 5.
- The revised Annex 11.

Guidance issued by other regulatory agencies such as WHO and FDA will be considered during the text revision to align expectations as far as possible.

Guidance on verifying transport routes and conditions in the supply chain will also be considered in the revision.

Further guidance will be added to the sections on documentation and validation types including transfer validation and qualification of equipment.

4. Recommendation

It is proposed that Annex 15 be updated to reflect changes in the regulatory and manufacturing environments. The scope of the project will be limited to Annex 15 but will take into account related changes in other GMP Chapters and Annexes as well as changes in other regulatory documents.

5. Proposed timetable

Preparation of draft concept paper	- September 2012 GMDP IWG meeting
Approval of draft concept paper	- October 2012
Released for consultation	- November 2012
Deadline for comments	- February 2013
Discussion in IWG	- June 2013
Discussion with other WPs	- June 2013 – September 2013
Proposed date for release of draft guideline	- December 2013
Deadline for comments	- March 2014

Re-discussion in GMDP IWG - May - September 2014

Expected date for adoption by Committee - October 2014

6. Resource requirements for preparation

Together with support from the EMA, there will a rapporteur from the UK and support from experts in other EU competent authorities (including Ireland, Germany, Italy and Portugal) and from the non-EU PIC/S Participating Authority (Canada). Given the key changes in the corresponding QWP document, there will be close working with members of that drafting group.

It is expected that most work will be completed by email and by teleconference.

Impact assessment (anticipated)

The updated Annex is intended to benefit both industry and regulators by incorporating new regulatory concepts, clarifying requirements and taking the opportunity to adopt a common approach with non-EU regulatory authorities.

No adverse impact on industry in terms of resources or costs is foreseen.

7. Interested parties

EMA (GMP/GDP IWG, QWP, BWP) and PIC/S

National Competent Authorities

Manufacturing industry

8. References to literature, guidelines, etc.

ICH Q8 (R2) Pharmaceutical development

ICH Q9 Quality Risk Management

ICH Q10 Pharmaceutical Quality System

PIC/S GMP Guide – Annex 15

FDA Guidance for Industry - Process Validation: General Principles and Practices

WHO Technical Report Series, No. 937, 2006